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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/600,911	08/01/2000	JERRY KANELLOS	47-139	2571

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EXAMINER
SNEDDEN, SHERIDAN

ART UNIT	PAPER NUMBER
1653	17

DATE MAILED: 07/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/600,911	KANELLOS ET AL.	
	Examin r	Art Unit	
	Sheridan K Snedden	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *none* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Response to Amendment

1. This Office Action is in response to Paper #15, filed 10 April 2003. Applicant's amendment of claims 1 and 14 is acknowledged. Applicant's addition of new claims 21-22 is acknowledged. Claims 1-22 are under examination.

Withdrawal of Objections and Rejections

2. The objections and/or rejections not explicitly restated or stated below are withdrawn.

Maintained Objections and Rejections

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Winkleman (US Patent 4,789,733), in view of Mosesson and Altieri *et al.* (US 20020131970 A1).

Winkleman teaches the enrichment of fibrinogen and Factor VIII from blood plasma fraction, especially cryoprecipitate (see abstract; regarding claim 2, 15, 19, and 21). This was achieved by the addition of at least 0.15 mg/ml of sulphated polysaccharide, especially heparin (regarding claim 7-9), to form a precipitate containing fibrinogen (see abstract; regarding claims 1 and 14, step (i)). In the paragraph bridging columns 5 and 6, Winkleman teaches this

precipitate containing fibrinogen may be further processes to extract fibrinogen. In examples 23 and 24 and column 6, Winkleman teaches how to further process a precipitate containing fibrinogen. Winkleman extracts fibrinogen (91% yield based on activity) from a precipitate using a saline solution (at least 0.1M NaCl or sodium chloride; regarding claims 3-5) and 2.2 M glycine (example 23; regarding claims 1 and 14, step (ii)). In example 24, the extracted FVII and fibrinogen is gel purified, lyophilized and heated for viral inactivation (regarding claims 11-12 and 17-18). The gel purification step would have removed SPS from the preparation.

Winkleman does not expressly teach the use of ϵ-aminocaproic acid (claim 6), NaCl concentrations of at least 0.2 M (claims 16, 20 and 22), the use of chromatographic techniques for the further purification of fibrinogen (claim 13), or the additional step of purifying fibrinogen away from fibronectin or Factor VIII (claim 14(iii)).

Mosesson teach the use of ϵ-aminocaproic acid in the preparation of fibrinogen. ϵ-aminocaproic acid is taught as enhancing the yield of fibrinogen by altering the solubility characteristics of fibrinogen. Additionally, Mosesson teaches the use of 0.3M NaCl in the preparation of fibrinogen. This method freed the composition of plasminogen.

Altieri *et al.* teach the use of a Sepharose.TM. 4B column (Pharmacia LKB, Piscataway, N.J.) to remove any possible contamination of the purified fibrinogen with fibronectin, the purified fibrinogen preparation which resulted in fibronectin-free fibrinogen (regarding claims 13 and 14(iii)).

Taken together, the above reference teaches the method of obtaining fibrinogen consistant with the method steps and reagents of claims 1-22. Thus, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to prepare fibrinogen

by first precipitating cryoprecipitate with sulphated polysaccharide precipitation, to extract fibrinogen using a solution of high ionic strength (0.3 M NaCl) and then to further purify the fibrinogen away from fibronectin. A person of ordinary skill in the art would have been motivated, and would have expected success, to combine the above steps and reagent as each step and reagents are well described in the prior art in methods of extraction and purification of fibrinogen. Thus, the claimed invention was within the ordinary skill in the art to make and use at the time it was made and was as a whole, *prima facie* obvious.

4. Applicant's arguments filed 10 April 2003, have been fully considered but they are not persuasive. Applicant urges that neither reference alone or in combination teaches or suggests the claimed invention. Applicant urges that Winkleman fails to teach the use of NaCl above the concentrations of saline. Applicant argues that the combination of conditions established as 0.1 M salt and eACA to recover fibrinogen is the result of the present inventors ingenuity and that the conditions could not have been predicted by one of ordinary skill in the art. These arguments are not convincing as Mosessom expressly teach the use of 0.3M salt and eACA in a method of extracting fibrinogen. As Winklemen teach and suggest to use of a solution of high ionic strength, it would have been it would have been obvious to the person of ordinary skill in the art at the time the invention was made to combine the teachings and use both 0.3M salt and eACA as taught by Mosesson.

Applicant further argue that Alteri does not teach how to re-dissolve this second precipitate and that Winkleman teach a Tris buffer for this step. These arguments are not convincing as a re-dissolving step is not claimed. A 3 step procedure is claimed that involves

precipitating with heparin, extraction with a salt solution of high ionic strength and further purification on an ion exchange column. These steps are taught by the cited references.

New Rejections

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 7-12, and 17-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Amrani (US Patent 4,278,594). Amrani teaches the separation of fibrinogen from blood plasma (see claim 1; regarding claims 1-2, 14, 21) in a two step process that involves precipitation and then extraction. Precipitation was achieved by the addition of sodium heparin, which Example 1 describes the heparin concentration diluted from 200 mg/ml (see claims 1-2; regarding claim 7-9), to form a precipitate containing fibrinogen (see claim 1, step (a)-(c); regarding claims 1, step (i)). The first step in the extraction process was to wash with dilute salts (see claim 1), which is described in Example 1 to be 0.1M NaCl (regarding claims 3-5), and then fibrinogen eluted and separated by chromatography, which would have resulted in the removal of SPS and further purification of fibrinogen (see claim 1, example 1; regarding claims 10, 13, 14(iii), 17). The gel purification step would have removed SPS from the preparation. Thus, the reference anticipates the claimed invention.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-22s are rejected under 35 U.S.C. 103(a) as being unpatentable over Amrani (US Patent 4,278,594), in view of Mosesson and Altieri *et al.* (US 20020131970 A1).

Amrani teaches the separation of fibrinogen from blood plasma (see claim 1; regarding claims 1-2, 14, 21) involving precipitation using a sulfated mucopolysaccaride, extraction with salt solution having an ionic strength with the range of 0.01-1, and then separating fibrinogen by chromatography. Precipitation was achieved by the addition of sodium heparin, which Example 1 describes the heparin concentration diluted from 200 mg/ml (see claims 1-2; regarding claim 7-9), to form a precipitate containing fibrinogen (see claim 1, step (a)-(c); regarding claims 1, step (i)). The first step in the extraction process was to wash with dilute salts (see claim 1), which is described in Example 1 to be 0.1 M NaCl (regarding claims 3-5), and then fibrinogen eluted and separated by chromatography, which would have resulted in the removal of SPS and further purification of fibrinogen (see claim 1, example 1; regarding claims 10, 13, 14(iii), 17). The gel purification step would have removed SPS from the preparation. Amrani teaches the use of chaotropic salts does not expressly teach the use of NaCl.

Mosesson teach the use of ϵ-aminocaproic acid in the preparation of fibrinogen. ϵ-aminocaproic acid is taught as enhancing the yield of fibrinogen by altering the solubility

characteristics of fibrinogen. Additionally, Mosesson teaches the use of 0.3M NaCl in the preparation of fibrinogen. This method freed the composition of plasminogen.

Altieri *et al.* teach the use of a Sepharose.TM. 4B column (Pharmacia LKB, Piscataway, N.J.) to remove any possible contamination of the purified fibrinogen with fibronectin, the purified fibrinogen preparation which resulted in fibronectin-free fibrinogen (regarding claims 13 and 14(iii)).

Taken together, it would have been it would have been obvious to the person of ordinary skill in the art at the time the invention was made to subtitute the use of chaotropic salts of high ionic strength with and NaCl solution and ϵ-aminocaproic acid in the preparation of fibrinogen. Thus, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to prepare fibrinogen by first precipitating cryoprecipitate with sulphated polysaccharide precipitation, to extract fibrinogen using a solution of high ionic strength (0.3 M NaCl) and then to further purify the fibrinogen away from fibronectin. A person of ordinary skill in the art would have been motivated, and would have expected success, to combine the above steps and reagent as each step and reagents are well described in the prior art in methods of extraction and purification of fibrinogen. Thus, the claimed invention was within the ordinary skill in the art to make and use at the time it was made and was as a whole, *prima facie* obvious.

Conclusion

7. No Claims are allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan K Snedden whose telephone number is (703) 305-4843. The examiner can normally be reached on Monday - Friday, 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (703) 308-2923. The fax phone number for regular communications to the organization where this application or proceeding is assigned is (703) 746-3975.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

SKS
June 30, 2003

SKS

Christopher S. Low
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SUPERVISORY PATENT EXAMINER
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